

Rewiring the Brain: The Promise and Peril of Neuroplasticity

Analysis by [Dr. Joseph Mercola](#)

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STORY AT-A-GLANCE

- › In the video "Rewiring the Brain: The Promise and Peril of Neuroplasticity," Brian Greene, a professor of physics and mathematics at Columbia University, interviews experts in the field of neuroplasticity about how human brain enhancement can help, and potentially harm, humanity
- › The panel includes neuroscientists Takao Hensch and John Krakauer, as well as entrepreneur Brett Wingeier, co-founder and CEO of Magnus Medical
- › They explore the potential of various tools, including pharmaceuticals, transcranial stimulation and even video games, to reopen critical learning windows and harness the brain's ability to rewire itself
- › Scientists are looking into how to reopen critical windows in the brain to enhance recovery from stroke, treat depression and even learn new skills, like attaining absolute pitch
- › The brain's development and learning pathways are highly complex; artificially manipulating these pathways might lead to unintended consequences with serious human health, ethical and social implications

In the video "Rewiring the Brain: The Promise and Peril of Neuroplasticity," Brian Greene, a professor of physics and mathematics at Columbia University, interviews experts in the field of neuroplasticity about how human brain enhancement can help, and potentially harm, humanity.¹

The panel includes neuroscientists Takao Hensch and John Krakauer, as well as entrepreneur Brett Wingeier, co-founder and CEO of Magnus Medical. They explore the potential of various tools, including pharmaceuticals, transcranial stimulation and even video games, to harness the brain's ability to rewire itself.

This capacity could potentially heal depression, reverse brain damage and enhance physical and cognitive abilities. However, there are important ethical considerations and potential risks of using such technologies to achieve superhuman enhancements.

Like Children, Adults May Benefit From Critical Windows of Brain Development

Hensch, who is a joint professor of neurology at Harvard Medical School at Children's Hospital Boston, and professor of molecular and cellular biology at Harvard's Center for Brain Science, has extensively researched the critical periods of brain development, particularly focusing on how these periods can be manipulated to promote neuroplasticity.

His work explores how early life experiences influence brain function, highlighting the role of specific inhibitory circuits in the brain that determine the timing of these critical periods.² These circuits can act as a sort of "brake" to the rewiring processes in the brain, making them essential targets for interventions aimed at recovering from neurological disorders or enhancing brain functions.

Hensch's research has revealed that the brain's critical periods, previously thought to be fixed, are actually plastic and reversible. This insight has significant implications for therapeutic strategies, such as treating epilepsy and autism spectrum disorders.

His laboratory uses a combination of molecular, cellular and systems neuroscience to explore these mechanisms, aiming to establish how a balance between excitatory and inhibitory signals can be manipulated to reopen these critical windows later in life.

This could potentially allow for the recovery of function or the enhancement of cognitive abilities in adults, which were once only possible in childhood. Hensch says:³

“We've known about critical periods or the importance of critical periods, malleability of the brain changing across development, for centuries – from Aristotle to Montessori to the present day – and this comes from careful observation of infants and children and their ability to acquire new skills at an astonishing rate ...

There are probably myriad number of critical periods ... brain function translates to particular circuits that change, whether you're talking about vision or hearing or speaking ... each one of those could have a slightly staggered window of plasticity.

And, in fact, there is a sense of hierarchy that perhaps the primary sensory areas, the first filters to the outside world, are shaped earliest and perhaps most stringently, which then feeds into multi-sensory areas that integrate the different kinds of input and ultimately build up a complex cognitive machine like the adult brain.”

Can Critical Windows Be Reopened to Enhance Brain Function?

Scientists are now looking into how to reopen critical windows in the brain to enhance recovery from stroke, treat depression and even learn new skills. Dr. John Krakauer, director of the Center for the Study of Motor Learning and Brain Repair at Johns Hopkins, explained that even traumatic brain injury can serve as a sort of reset button that reopens brain plasticity:⁴

“You get most recovery from all sorts of brain injury early in animal models and in humans ... we did a very slightly freaky experiment in the mouse where we basically gave a mouse a stroke and then delayed its training, and it never really got back to normal behavior.

We found also that if you started the training very soon after the stroke – in other words you don't wait a week you wait just a day – then the efficacy of the training was much greater, to the point that you couldn't actually tell the difference between ... before and after the stroke.

Now the really freaky thing is if you did the original experiment and waited a week and then gave a second stroke – in other words you actually made the mouse worse – but you now didn't wait, you actually recovered completely from the first stroke. So, in other words, a very profound demonstration of being able to manipulate a critical period by injuring the brain.

In terms of why that should be the case, it seems to me it's only sort of logical and parsimonious to imagine that there are repair mechanisms in the brain ... Just like you cut your skin, break a bone, damage neural tissue, there's going to be some repair process set in place that will have some overlap with the kind of processes going on during development.”

Wingeier's company, Magnus Medical, is also attempting to rewire the brain, using a form of transcranial magnetic stimulation called intermittent theta-burst stimulation (iTBS). This method applies magnetic pulses to the brain to influence neuronal activity, targeting specific brain regions that are involved in mood regulation, such as the dorsolateral prefrontal cortex.

The goal is to modulate the neural circuits that contribute to depression, particularly in individuals who haven't responded to other treatments. Research published in *The American Journal of Psychiatry* revealed that Magnus' Stanford neuromodulation therapy, which was previously referred to as Stanford accelerated intelligent neuromodulation therapy, or SAINT, was useful for depression.⁵

In the double-blinded, randomized controlled trial, 79% of those who received the treatment entered remission from their depression compared to 13% in the placebo group.⁶ Wingeier explains that similar techniques could be used for other health conditions and even to enhance human performance:⁷

"I've spent about two decades building technology to stimulate and to enhance, to treat, the brain, mostly on the medical side. I've worked in epilepsy, done some work in Parkinson's disease, cluster headache and now, at Magnus Medical, in a new treatment for depression ... and on the plasticity and human performance side at a company called Halo Neuroscience.

The mechanisms behind plasticity are complex ... but there's this electrical component to brain activity and an electrical component to creating plasticity ... we think enhancing plasticity with neurostimulation – electrical nerve stimulation – whether it's pulses that are timed or waveforms that are geared to interact with this underlying brain activity, it's possible to modulate plasticity."

Rewiring the Brain Gets Adults Closer to Perfect Pitch

Perfect pitch, also known as absolute pitch, is typically acquired in early life, and there is evidence suggesting that the development of this ability is strongly linked to early musical training. While it's typically believed that once this critical period is over, the ability to learn perfect pitch is lost, Hensch's research shows the use of histone-deacetylase inhibitors (HDAC inhibitors) may reopen the critical period of learning for absolute pitch.⁸

The study found adult men who took the HDAC inhibitor valproate (VPA) learned to identify pitch significantly better than those taking a placebo. The implication is that one day drugs could become commonplace for those looking to learn something new, such as another language or playing a musical instrument.

"Certainly this possibility is out there," Hensch says, "and I'm sure many college campuses are already dealing with this kind of situation." He continues:⁹

"There is most recently in this category of thinking, the use of psychoactive drugs as a way to reopen critical periods. There was a very nice study from Hopkins, in fact, that published evidence of a social critical period in rodents and that this window could be reopened by the drug MDMA, or ecstasy.

This is not to advocate rampant drug use but it's to show a proof of principle that with a very well-measured hypothesis-driven approach we might be able to tap the neuromodulatory systems that are dampened with age through this enhancement. But that alone is not going to produce plastic change. It requires the training to go with it."

Krakauer and his team at Johns Hopkins, meanwhile, is exploring neuroplasticity enhancement via immersive environments like video games. By learning to control the movements of a dolphin, for instance, stroke patients may experience better recovery.

The idea behind the game is to create an enjoyable and immersive environment that motivates patients to perform repetitive movements, which are crucial for recovery but can often be tedious. By simulating the control of a dolphin, the game engages patients in a way that traditional physical therapy might not.

This type of gamified therapy can potentially make the rehabilitation process more appealing and effective, helping patients regain motor functions more quickly. In fact, research suggests the simulator may be twice as effective as conventional rehabilitation for stroke patients.¹⁰

"If you just see yourself trying to open a cupboard or lift up a cup you are going to try to do it the way you used to do it and you are going to get depressed when you can't," Krakauer told Sky News.

"We are putting you in an environment that can't be compared to anything you have ever done, and so you are free to explore and free to feel good. You want an alternative reality where you don't think about your limitations."¹¹ Such games are also being explored to enhance well-being in adults aged 65 and older.¹²

Warning Flags Raised in the Quest to Build a More Perfect Human

While the potential to reopen critical learning windows and enhance recovery from brain injury or cognitive abilities in humans is exciting, it also raises multiple red flags. The brain's development and learning pathways are highly complex. Artificially manipulating

these pathways might lead to unintended consequences, including abnormal brain development or function or increased risk of neurological disorders like Alzheimer's disease.

The ability to enhance cognitive abilities through neuroplasticity raises ethical questions about fairness, accessibility and potential misuse. Frequent reliance on technological interventions to enhance brain function might also lead individuals to depend excessively on external aids, potentially diminishing the brain's natural ability to cope with challenges and adapt through intrinsic mechanisms.

Not to mention, altering a person's cognitive or sensory abilities could have profound psychological impacts, including changes in personal identity or self-perception. "I'm reminded of a quote by Charles Baudelaire, a French poet who once said genius is nothing more nor less than childhood recovered at will," Hensch says, continuing:¹³

"Trying to refine that child-like state, many artists have talked about this as well, but I think the key in that quote is 'at will' and the ability to do it in a regulated way ... [as for] what the risks might be ... we've all gone through critical periods shaping who we are.

Our identities are formed in childhood and our experiences, our cultural background, the languages we speak, the skills we have – if we were to actually be able to reverse all of that, wouldn't we lose our self?"

Krakauer also worries about the race to extend such technologies beyond medical uses and into the consumer space, well before the full ramifications are understood:¹⁴

"I am extremely worried about a particular West Coast techno-utopianism that America suffers from where basically the technological tale wags the biological dog. And the real interest is to try and sell and to try and make money by making people think they're going to be bionic or they're going to be like the Matrix ... I think that we have to be super careful and spend a lot more time doing the trials and the science.

Yes, when there are diseases which are really refractory to drugs, like depression, and the spinal cord injury – spinal cord stimulation is doing amazing things for walking – yes, I'm all for that.

But I am just in general very concerned about the premature jump to consumerism and also the bad faith of claiming that you're doing this for medicine, but really what you're desperately trying to do is get the consumer version right and that is a trend that I am very concerned about.”

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